Amendments to the Claims

Please cancel Claims 2, 4 and 10. Please amend Claims 1, 5, 11, 12, 16 and 17. Please add Claims 18 and 19. The Claim Listing below will replace all prior versions of the claims in the application:

Claim Listing

1.   (Currently amended) An *in vitro* method of defining the differentiation grade of a tumor with genes and/or proteins selected by statistical analyses based on expression levels or patterns of the genes and/or proteins of human <u>liver</u> tumor tissues obtained from ~~cancer patients~~ <u>non-cancerous liver (L0), pre-cancerous liver (L1), well differentiated hepatocellular carcinoma (HCC) (G1), moderately differentiated HCC (G2) and poorly differentiated HCC (G3)</u>, comprising:

   (i) determining said expression levels or patterns of genes and/or proteins of said human <u>liver</u> tumor tissues from ~~at least two~~ <u>five</u> different grades of tumor; and

   (ii) selecting a set of genes and/or proteins ~~associated with said at least two different grades of tumor differentiation~~ <u>that are differentially expressed between (1) L0 and L1, (2) L1 and G1, (3) G1 and G2, and (4) G2 and G3</u>, wherein the genes and/or proteins are selected <u>by a supervised learning method</u> in descending order of Fisher ratio ~~and wherein the Fisher ratio is determined without the use of a prior probability~~.

2-4.   (Canceled)

5.   (Currently amended) The *in vitro* method according to claim [[4]] <u>1</u>, wherein the assay is selected from the group consisting of DNA microarray, reverse transcription polymerase-chain reaction, northern blotting, *in situ* hybridization, ribonuclease protection assay, western blot, enzyme-linked immunosorbent assay and protein array.

6.   (Canceled)

7.   (Previously presented) The *in vitro* method according to claim 1, wherein the selected genes and/or proteins are in a number that is between 40 and 100.

8.   (Previously presented) The *in vitro* method according to claim 1, wherein the selected genes and/or proteins are in a number that is between 35 and 45.

9.   (Previously presented) The *in vitro* method according to claim 8, wherein the number of the genes and/or proteins is 40.

10.   (Canceled)

11.   (Currently amended) An *in vitro* method of defining the differentiation grade of a hepatocellular carcinoma (HCC) tumor, the method comprising the steps of:

    (a)   determining expression levels or patterns of genes and/or proteins in human liver tissues from non-cancerous liver, pre-cancerous liver, well differentiated hepatocellular carcinoma (HCC) tumor, moderately differentiated HCC tumor and poorly differentiated HCC tumor;

    (b)   determining a number of genes and/or proteins to define the differentiation grade of a tumor; and

    (c)   selecting genes and/or proteins <u>by a supervised learning method</u> in descending order of Fisher ratio in the number determined in step (b), wherein the Fisher ratio is applied in comparison of said gene and/or protein expression levels or patterns determined in step (a) between (1) non-cancerous liver and pre-cancerous liver, (2) pre-cancerous liver and well differentiated hepatocellular carcinoma (HCC), (3) well differentiated HCC and moderately differentiated HCC, and (4) moderately differentiated HCC and poorly differentiated HCC, ~~wherein the Fisher ratio is determined without the use of a prior probability~~[[,]] thereby defining the differentiation grade of a HCC tumor.

12.   (Currently amended) An *in vitro* method of determining the differentiation grade of a hepatocellular carcinoma (HCC) tumor, the method comprising the steps of:

(a)   determining expression levels or patterns of genes and/or proteins in human liver tissues from non-cancerous liver, pre-cancerous liver, well differentiated hepatocellular carcinoma (HCC) tumor, moderately differentiated HCC tumor and poorly differentiated HCC tumor;

(b)   determining a number of genes and/or proteins to define the differentiation grade of a tumor;

(c)   selecting genes and/or proteins by a supervised learning method in descending order of Fisher ratio in the number determined in step (b), wherein Fisher criterion is applied in comparison of said gene and/or protein expression levels or patterns determined in step (a) between (1) non-cancerous liver and pre-cancerous liver, (2) pre-cancerous liver and well differentiated hepatocellular carcinoma (HCC), (3) well differentiated HCC and moderately differentiated HCC, and (4) moderately differentiated HCC and poorly differentiated HCC[[,]] wherein the Fisher ratio is determined without the use of a prior probability;

(d)   designing a minimum distance classifier with expression data of the genes and/or proteins selected in step (c);

(e)   applying the minimum distance classifier designed in step (d) to expression levels or patterns of the genes and/or proteins selected in step (c) of an unknown sample whose grade of differentiation is to be determined;

(f)   generating a self-organizing map with expression data of the genes and/or proteins selected in step (c); and

(g)   applying the self organizing map generated in step (f) to said expression levels or patterns of the genes and/or proteins selected in step (c) of the unknown sample whose grade of differentiation is to be determined,
       thereby determining the differentiation grade of a tumor.

13.   (Withdrawn) A kit for carrying out the method according to claim 1, the kit comprises DNA chips, oligonucleotide chips, protein chips, probes or primers that are necessary for

effecting DNA microarrays, oligonucleotide microarrays, protein arrays, northern blotting, RNase protection assays, western blotting, and reverse transcription polymerase-chain reaction to examine the expression of the genes and/or proteins selected by the statistical analyses in claim 1.

14.   (Withdrawn) Use of genes and/or proteins according to any one of claim 1 for screening anti-cancer agents.

15.   (Withdrawn) Use of antibodies specific to genes and/or proteins according to claim 1 for treating tumors in different grades.

16.   (Currently amended) The *in vitro* method according to claim 1, further comprising the steps of[[:]]

    (i) designing a minimum distance classifier with expression data of the genes and/or proteins selected in Claim 1[[;]]

    ~~(ii) determining expression levels or patterns of the genes and/or proteins selected in Claim 1 in a liver tissue of an unknown sample whose grade of differentiation is to be determined; and~~

    ~~(iii) applying the minimum distance classifier to the expression levels or patterns of the genes and/or proteins of the unknown sample whose grade of differentiation is to be determined~~[[,]]

    ~~thereby determining the differentiation grade of a tumor~~.

17.   (Currently amended) The *in vitro* method according to claim ~~16~~ 1, further comprising the steps of[[:]]

    (i) generating a self-organizing map with expression data of the genes and/or proteins selected in Claim 1[[;]]

    ~~and~~

(ii) applying the self-organizing map to said expression levels or patterns of the selected genes and/or proteins of the unknown sample whose grade of differentiation is to be determined.

18.   (New) An *in vitro* method of diagnosing the differentiation grade of hepatocellular carcinoma (HCC) in a liver tissue, the method comprising the steps of:

   (i) obtaining a liver tissue whose differentiation grade is to be diagnosed;

   (ii) determining expression levels or patterns of the genes and/or proteins selected in Claim 1 in the liver tissue whose differentiation grade is to be diagnosed; and

   (iii) applying the minimum distance classifier generated in Claim 16 to said expression levels or patterns of the genes and/or proteins determined in step (ii), thereby diagnosing the differentiation grade of HCC in a liver tissue.

19.   (New) An *in vitro* method of diagnosing the differentiation grade of hepatocellular carcinoma (HCC) in a liver tissue, the method comprising the steps of:

   (i) obtaining a liver tissue whose differentiation grade is to be diagnosed;

   (ii) determining expression levels or patterns of the genes and/or proteins selected in Claim 1 in the liver tissue whose differentiation grade is to be diagnosed; and

   (iii) applying the self-organizing map generated in Claim 17 to said expression levels or patterns of the genes and/or proteins determined in step (ii), thereby diagnosing the differentiation grade of HCC in a liver tissue.